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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/588,818	08/23/2006	Takahide Nishi	06439/HG	2782

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EXAMINER	
BLAKELY III, NELSON CLARENCE	
ART UNIT	PAPER NUMBER
1614	
MAIL DATE	DELIVERY MODE
06/16/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/588,818	NISHI ET AL.	
	Examiner	Art Unit	
	NELSON C. BLAKELY III	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 March 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,8 and 18-42* is/are pending in the application.

4a) Of the above claim(s) *19 and 21-41* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,8,18,20 and 42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *See Continuation Sheet*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :08/09/2006, 09/25/2006, 11/10/2006 and 01/15/2008.

DETAILED ACTION

Application Status

Claims 1-6, 8 and 18-42 of the instant application are pending. Claims 19 and 21-41 are withdrawn pursuant to Applicant's Response, filed 03/31/2010. Accordingly, instant claims 1-6, 8, 18, 20 and 42, drawn to a method for suppressing the number of peripheral blood lymphocytes comprising administering to a human in need thereof a pharmaceutically effective amount of a compound having a formula (I), a pharmacologically acceptable salt thereof, or a pharmacologically acceptable ester thereof, are presented for examination on their merits.

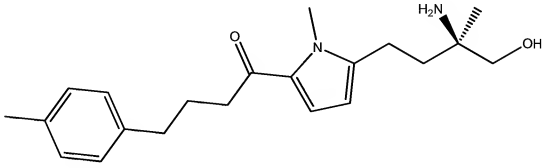
Election/Restrictions

Applicant's election ***with*** ***traverse*** of (2R)-2-amino-2-methyl-4{1-methyl-5-[4-(4-methylphenyl)butanoyl]pyrrol-2-yl}butan-1-ol, in the reply filed on 03/31/2010, is acknowledged. The traversal is on the ground(s) that the election requirement is not a species requirement of the type set forth in MPEP §803.02 entitled "MARKUSH CLAIMS".

This is not found persuasive. As set forth on page 6 of the Office Action mailed 03/18/2010, the R_3 substituents, e.g., $-CH_3$ and –CN, do not share a technical relationship, such as common biological, physical or chemical properties.

The requirement is still deemed proper and is therefore made FINAL.

It is acknowledged that Applicant elected wherein the disclosed compound of formula (I) is



(2R)-2-amino-2-methyl-4-{1-methyl-5-[4-(4-methylphenyl)butanoyl]pyrrol-2-yl}butan-1-ol.

Claims 19 and 21-41 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected subject matter, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 03/31/2010.

Priority

Receipt is acknowledged of the certified copy of JP 2004-048205, filed 02/24/2004, submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file. Applicant cannot rely upon the foreign priority papers to overcome the rejection(s) set forth *infra* because an English translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

Information Disclosure Statement

The Information Disclosure Statements, filed 08/09/2006, 09/25/2006, 11/10/2006 and 01/15/2008, are acknowledged.

The Information Disclosure Statement, filed 01/15/2008, fails to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 for the following reasons:

a) The foreign patent documents EP1002792 and EP0492497, on page 3, were submitted on page 1 of the IDS filed 09/25/2006, and, respectively, at least the abstract is not in English;

b) U.S. patent document nos. 5,604,229 and 6,605,744, on page 10, were first mentioned on page 2 and 9, respectively, of the instant IDS ; and

c) U.S. patent document no. 6,214,873, on page 11, was first mentioned on page 2 of the instant IDS, and the number "1" was inserted in the foreign patent document no. "WO 0/01978" as "WO 01/01978". See the "*" at the bottom of the instant page.

Only foreign patent document no. EP0492497 has been placed in the application file, but the information referred to therein has not been considered as to the merits. The additional documents mentioned *supra* are duplicates or contain typographical errors that were amended by the Examiner, and have been considered. Applicant is advised that the date of any re-submission of any item of information contained in this Information Disclosure Statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609.05(a).

Applicant's Amendment

Applicant's Preliminary Amendment, filed 08/09/2006, wherein the specification and claims 1-6, 8 and 18 are amended, claims 7 and 9-17 are canceled, and claims 19-42 are added, is acknowledged. Applicant's Preliminary Amendment, filed 08/23/2006, wherein the specification is amended, is acknowledged.

Specification

Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

The abstract of the disclosure is objected to use of legal phraseology, "comprising" (line 6).

Correction is required. See MPEP § 608.01(b).

The disclosure is objected for the following informality:

On page 72, lines 4 and 5, of the instant specification, Applicant recites "...is 0.0001 mg/kg to 1.0 mg/kg, and preferably 0.001 mg/kg/**day** to 0.1 mg/kg.".

Confusingly, because only one dosage amount recites "…/day…", it is unclear to the Examiner whether or not the aforementioned dosage ranges are restricted to once daily, or multiple times per day, administration.

The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Appropriate correction is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-6, 8, 18, 20 and 42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nishi *et al.* (International Publication No. WO 03/059880A1; U.S. Patent Application Publication No. 2005/0043386A1 is supplied as an English language equivalent; both cited by Applicant), in view of Budd *et al.* (U.S. Patent Application Publication No. 2002/0086832A1).

With regard to instant claims 1-6, 8, 18, 20 and 42, Nishi *et al.* disclose, in the Abstract, amino alcohol compounds having excellent immunosuppressive activity, pharmacologically acceptable salts thereof and pharmacologically acceptable esters thereof. In reference claims 225 and 233, pages 199 and 200, Nishi *et al.* a method for the treatment of an autoimmune disease, and rejection caused by transplantation of an organ or skin, in a human in need thereof, which comprises administering to said human a pharmaceutically effective amount of a compound, a pharmacologically acceptable salt, or a pharmacologically acceptable ester according to claim 181, for example, wherein the compound is 2-amino-2-methyl-4-{1-methyl-5-[4-(4-methylphenyl)butanoyl]pyrrol-2-yl}butan-1-ol. See lines 15 and 16 of reference claim 181. Nishi *et al.* disclose, in paragraph **[0596]**, page 24, wherein a preferred organic

acid salt of general formula **(I)** is fumarate. See instant claims 1-6, 8, 20 and 42. In paragraph **[1600]**, page 151, Nishi *et al.* disclose wherein the dosage varies depending on the symptoms, age, etc., of the human adult patient, and in the case of oral administration, it is desirable to administer from 0.05 mg to 200 mg per one time, up to six times, per day. Applicant recites in instant claim 18 a dose of 0.0001 mg/kg/day to 1 mg/kg/day. Considering that the average human adult weighs 70 kg, a skilled artisan, at the time of the invention, would have envisaged a claimed dosage amount from 0.007 mg/day to 70 mg/day (e.g., 1 mg/kg/day x 70 kg = 70 mg/day). Accordingly, the amounts disclosed by Nishi *et al.*, e.g., 0.05 mg, meet the instant claim.

Nishi *et al.* fail to disclose specifically wherein the method suppresses the number of peripheral blood lymphocytes (instant claims 1 and 42). However, Budd *et al.* disclose in the Abstract the use of inhibitors for treating diseases or disorders caused by a hyperproliferation of peripheral blood lymphocytes, wherein the inhibitors suppress the immune system. In paragraphs **[0012]** and **[0014]**, page 2, Budd *et al.* disclose wherein the inhibitors treat diseases, disorders or pathophysiological conditions in which the immune defenses are directed against the body's own structures, preferably autoimmune diseases. In the instant excerpt, Budd *et al.* disclose wherein the inhibitor is advantageous if a fundamental suppression of the immune system is desired, wherein the immune response is supported by peripheral blood lymphocytes.

Therefore, a skilled artisan would have envisaged the instantly claimed method for suppressing the number of peripheral blood lymphocytes (PBL), as disclosed by Budd *et al.*, with a compound of formula **(I)**, e.g., as disclosed by Nishi *et al.*, wherein

the immune response, e.g., autoimmune disease, is supported by PBL. One of ordinary skill in the art would have been motivated to combine the teachings of the aforementioned references when seeking a method of suppressing an immune response without serious side effects, which increases patient compliance. It would have been obvious to one of ordinary skill in the art, at the time of the invention, because the combined teachings of the prior art are fairly suggestive of the claimed invention.

Accordingly, the instant invention, as claimed in claims 1-6, 8, 18, 20 and 42, is *prima facie* obvious over the combination of the aforementioned teachings.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to NELSON C. BLAKELY III whose telephone number is (571) 270-3290. The examiner can normally be reached on Mon - Thurs, 7:00 am - 5:30 pm (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Phyllis G. Spivack/
Primary Examiner, Art Unit 1614

June 14, 2010

/N. C. B. III/
Examiner, Art Unit 1614